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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/444,221	11/19/1999	BRIAN R. MURPHY	17634-000513	8357

7590 06/26/2002

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EXAMINER
BRUMBACK, BRENDA G

ART UNIT	PAPER NUMBER
1642	18

DATE MAILED: 06/26/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/444,221	Applicant(s) MURPHY ET AL.	
	Examiner Brenda G. Brumback	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *63-147* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *63, 90, 93-94, 100-101, 103, 114-124, 127, 131, and 133* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continuation of Disposition of Claims: Claims withdrawn from consideration are 64-89,91,92,95-99,102,104-113,125,126,128-130,132 and 134-147.

DETAILED ACTION

This action is responsive to the amendment filed 04/05/2002. Claims 90, 101, 114, and 116 were amended.

Pending claims are 63-147.

Claims 63, 90, 93-94, 100-101, 103, 114-124, 127, 131, and 133 are under examination on the merits.

This application contains claims 64-89, 91, 92, 95-99, 102, 104-113, 125-126, 128-130, 132, and 134-147, drawn to an invention nonelected in Paper No. 11. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Objections

The objections to claims 101 and 114 are withdrawn pursuant to applicant's amendment thereof.

Claim Rejections - 35 USC § 112

The rejections of claims 90 and 115-116 under 35 U.S.C. 112, second paragraph, are withdrawn due to applicant's amendment thereof.

The rejection of claim 101 under 35 U.S.C 112, first paragraph, for the deposit requirement is maintained. While applicant's submission of the deposit receipts from the ATCC is acknowledged, assurance of compliance in the form of a declaration or averment under oath is required (see the previous Office action for a suggested format, page 4) (see MPEP 2400, especially 2403, 2404.01, 2404.02, and 2404.03). Additionally, the deposit must be referred to in the body of the specification by deposit (accession) number, name and current address of the depository, and the complete taxonomic description.

The rejection of claims 117-124 under 35 U.S.C. 112, first paragraph, as not enabled for vaccine compositions to induce protection in a human individual against subsequent RSV infection is maintained. Applicant's arguments have been fully considered but they are not persuasive for the following reasons.

Applicant argues that the artisan would not expect that useful vaccines are to be 100% effective in a single dose for all populations covering all potential variants of a targeted pathogen and that development of a live-attenuated vaccine would not constitute undue experimentation. The present rejection, however, is based on general teachings of unpredictability found in the art regarding the overall lack of efficacy for RSV vaccine compositions, not on a lack of absolute predictability in conferring protective immunity in every case. The art teaches that such vaccines are not effective in conferring protective immunity in any significant proportion of any human population to any reasonable degree. Applicant has provided no evidence to the contrary.

Regarding the issue of animal model data, applicant argues that the demonstration of immunogenicity sufficient to elicit an immunogenic response in murine subjects is sufficient to be predictive in humans of an immunoprotective response. Applicant further submits published articles describing the use of rodent models, followed by non-human primate trials, as a widely accepted course of validation. However, none of the references submitted by applicant teach that the mouse model is predictive of RSV vaccine efficacy in humans. In fact, Murphy et al. (Virus Research 32 :13-36, 1994, of record and also submitted with applicant's response), teach "that it is relatively easy to protect rodents and monkeys which are only semipermissive for RSV infection, but it is more difficult to protect the seronegative chimpanzee, a fully permissive host" (sentence bridging pages 23-24). The art is replete with teachings of the unpredictability of the efficacy of RSV vaccines in the human ppulation. Applicant's disclosure and working examples, which are limited to eliciting an immunogenic response in mice, lack sufficient guidance as to how overcome these teachings of unpredictability.

Claim Rejections - 35 USC § 103

The rejection of claims 63, 93, 94, 114, 115, 117, 121, 122-124, 127, 131, and 133 under 35 U.S.C. 103(a) as being unpatentable over Collins et al. in view of any of Marr et al., Chen et al., or Doyle et al.; the rejection of claims 90, 100-101, and 103 under 35 U.S.C. 103(a) as being unpatentable over Collins et al. in view of any of Marr et al., Chen et al., or Doyle et al. and further in view of any of Crowe 1994 #1, Crowe 1994 #2, Crowe et al. 1995 or Murphy et al.; and the rejection of claims 116, 118-120, and 123-124 under 35 U.S.C. 103(a) as being unpatentable over Collins et al. in view of any of Marr et al., Chen et al., or Doyle et al. and further in view of Randolph et al. are all maintained. Applicant's arguments have been fully considered but they are not persuasive.

Applicant argues that Collins et al. is a defective primary reference because Collins et al. does not forecast a reasonable expectation of success for introducing significant genetic changes to yield live-attenuated vaccine candidates and as such constitutes an invitation to experiment. Applicant's claims for purposes of the present rejection, however, are not limited to vaccine strains for eliciting protective immunity in a human host due to significant genetic changes, but rather encompass isolated recombinant RSV, wherein a modification is introduced within the genome comprising introduction of one or more translation termination codons for reduction or ablation of a selected gene (see page 9 or the previous Office action). Such modifications are not limited to significant genetic changes yielding vaccine strains. While Collins et al. may not be enabling for production of effective RSV vaccine strains, it is fully enabling for introduction of defined changes into infectious RSV particles (see the abstract). Applicant is reminded that absolute predictability is not required, but rather a reasonable expectation of success. The teaching in Collins of production of a recombinant human RSV from cloned cDNA provides such a reasonable expectation of success. In fact, Collins et al. support such a reasonable expectation of success by teaching that "it should thus be possible to introduce defined changes into infectious RSV" (the

abstract) and "The ability to introduce defined mutations into infectious RSV should have many applications ..." (page 11566, the paragraph bridging columns 1 and 2).

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Brumback whose telephone number is (703) 306-3220. If the examiner can not be reached, inquiries can be directed to Supervisory Patent Examiner Anthony Caputa whose telephone number is (703) 308-3995. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Examiner Brenda Brumback, Art Unit 1642 and should be marked "OFFICIAL" for entry into prosecution history or "DRAFT" for consideration by the examiner without entry. The Official FAX telephone number is (703) 872-9306 and the After Final FAX telephone number is (703) 872-9307. FAX machines will be available to receive transmissions 24 hours a day. In compliance with 1096 OG 30, the filing date accorded to each OFFICIAL fax transmission will be determined by the FAX machine's stamped date found on the last page of the transmission, unless that date is a Saturday, Sunday or Federal Holiday with the District of Columbia, in which case the OFFICIAL date of receipt will be the next business day.

BB
June 25, 2002

Brenda Brumback
Primary Examiner